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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/000,297	12/04/2001	Shu Wang	11042-003	8915

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08/10/2005

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EXAMINER

BAXTER, JESSICA R

ART UNIT

PAPER NUMBER

3731

DATE MAILED: 08/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/000,297

Applicant(s)

WANG ET AL.

Examiner

Jessica R. Baxter

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-38 and 40-133 is/are pending in the application.
- 4a) Of the above claim(s) 1-21, 23, 29, 42-46, 50, 51, 57-97, 105, 118, 119, 121, 122, 126, 127 and 133 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22, 24-28, 30-38, 40, 41, 47-49, 52-56, 98-104, 106-117, 120, 123-125 and 128-132 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 June 2002 and 30 May 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- 1) ☐ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election of species in the reply filed on 18 April 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant indicated that the species weren't grouped properly. However, the applicant failed to indicate the supposed errors.
2. Claims 29,42-46, 50, 51, 57, 105, 118, 119, 121, 122, 126, 127 and 133 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Response to Amendment

3. The declaration under 37 CFR 1.132 filed 08 January 2004 is insufficient to overcome the rejection of claims 22,24-27,47-49 based upon PG-PUB 2002/0155092 as set forth in the last Office action because: the declaration is not clear as to what part of the reference is the applicant's. The declaration states that the compound was invented by the applicant, this is not sufficient to overcome the rejection of a nerve guide. See MPEP 715.01 and 716.10.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 99, 100, 101, 102, are rejected under 35 U.S.C. 102(e) as being anticipated by PG-PUB 2002/0155092 to Leong et al.

Leong discloses (0649) a tube for regenerating nerve tissue. The tube can contain a polyphosphoester) polymer (a polymer containing at least 1 phosphoester bond.) In paragraph (631) the range of polymer's molecular weight is disclosed to be from 2,000 - 20,000 AMU. The Leong system is designed as a drug delivery system. The protein delivery system comprises microspheres that contain protein wherein said protein will be inherently released from the microspheres progressively. The microspheres are made from a poly(phosphoester) polymer.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 22, 24-27, 40, 41, 47-49, 52, 53, 56, 115, 116, 117, 120, 123, 124, 125 and 128, 129, 131 are rejected under 35 U.S.C. 103(a) as being unpatentable over PG-PUB 2002/0155092 to Leong et al. in view of PG-PUB 2002/0071828 to Peulve et al.

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Leong discloses (0649) a tube for regenerating nerve tissue. The tube can contain a poly(phosphoester) polymer (a polymer containing at least 1 phosphoester bond.) Leong discloses the claimed invention except for the gene delivery system. Peulve teaches that gene delivery systems are used with in order to improve nerve tissue regrowth (Paragraph 0079). It would have been obvious to one having ordinary skill in the art at the time the invention was made to provide the device of Leong with a gene delivery system in order to help stimulate nerve tissue regrowth.

In paragraph (631) the range of polymer's molecular weight is disclosed to be from 2,000 - 20,000 AMU. Regarding claim 47, the Leong system is designed as a drug delivery system. Regarding claims 48 and 49, the protein delivery system comprises microspheres that contain protein wherein said protein will be inherently released from the microspheres progressively. The microspheres are made from a poly(phosphoester) polymer.

The Leong-Peulve device discloses (Peulve '828 (Paragraph 00412) the use of a complex of DNA and a cationic polymer or lipid loaded into a cuff.

Regarding claims 41, 52, and 53, the Leong-Peulve device discloses the size of the complex's particles to be 5 microns and at the time of the invention it would have been obvious to one having ordinary skill in the art to vary the size of the particles to change the rate of the dissolution of the microparticles to 10 microns to enable the conduit to be useful for delivery of different proteins that would change the rate of dissolution.

Regarding claim 55, the Leong-Peulve device doesn't disclose the length of protein to be loaded per length of conduit. It would have been an obvious matter of design choice to modify the Peulve-Leong device to have the 10 microns of protein to be loaded per 10 mm of conduit since the applicant has not disclosed this loading procedure would solve any

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stated problem or is for any particular purpose and it appears that the undisclosed amount of protein added by Peulve would perform equally well.

Regarding claim 56, the Leong-Peulve device discloses that BDNF (Peulve '828 (Paragraph 024)) is a preferred neutrophin to use in the gene delivery system of Peulve.

8. Claims 27, 28, 30-38, 98, 103-114 are rejected under 35 U.S.C. 103(a) as being unpatentable over PG-PUB 2002/0155092 to Leong et al. in view of Peulve et al. '828, as applied above, further in view of U.S. Patent No. 5,026,381 to Li.

Regarding claims 27-28, Leong, as modified, discloses the claimed device except for the porosity of the material. However, it is well known in the art to vary the porosity of a material to change the amount of time the material takes to dissolve invitro. At the time of the invention it would have been obvious to one having ordinary skill in the art to make the porosity 8% or 35% to modify the amount of time the material requires for complete dissolution.

Regarding claims 30-33, Leong does not disclose the wall thickness of the nerve guide, but nerve guide conduits typically have a wall thickness of about 0.3mm (which includes thicknesses from .21 mm to .39mm). Li '381 teaches the thickness of nerve guides, (t-fypically for a 1 mm x .5cm conduit having an overall wall thickness of about .3mm.. ." At the time of the invention it would have been obvious to one having ordinary skill in the art to make the wall thickness of the Leong device about .3 mm because Li teaches this size is the typical size of a nerve guide.

Regarding claims 34-37, the combined Leong device discloses a device with many layers of material (figure 1 of Li shows a multi-layered material). The thickness of the

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individual layers is not disclosed. It would have been an obvious matter of design choice to modify the Leong-Li device to have a wall layer thickness of 25 micrometers since the applicant has not disclosed the layer thickness of 25 micrometers would solve any stated problem or is for any particular purpose and it appears that the undisclosed layer thickness of Li would perform equally well.

Regarding claim 38, the combined Leong device does not disclose that the outer surface of the wall has greater microporosity than the luminal surface of the conduit. It would have been an obvious matter of design choice to modify the Leong-Li device to have a wall layer thickness of 25 micrometers since the applicant has not disclosed the layer thickness of 25 micrometers would solve any stated problem or is for any particular purpose and it appears that undisclosed microporosity relationship between the said surface of the Leong device would perform equally well.

9. Claim 54 and 130 is rejected under 35 U.S.C. 103(a) as being obvious over in Leong '092 in view of Peulve et al. '828.

Leong discloses the nerve conduit should release protein from the microspheres, but does not disclose for what temporal duration the microspheres should release the protein. Providing the nerve cells with a long, constant source of protein will improve the regenerative qualities of the procedure. At the time of the invention it would have been obvious to one having ordinary skill in the art to modify the Leong device so that microspheres will dissolve very slowly thus releasing the protein for three months or longer, and thereby improving the regenerative qualities of the procedure. Also, methods of modifying the longevity of the microsphere are well known in the art. Increasing porosity or surface area of the sphere will result in faster dissolution times.

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10. Claims 22, 24-28, 30, 31, 40, 47-49, 54-56, 99-104, 106, 107, 115, 116, 123-125, and 130-132 are rejected under 35 U.S.C. 103(a) as being obvious over Peulve et al. (Peulve) 2002/007 1828 in view of U.S. Patent No. 5,256,765 to Leong.

Peulve discloses making a nerve guide polymer in the shape of a tube. Peulve in (001 81 discloses that a gene delivery system can be incorporated into the nerve guide. Puelve lists materials one could use to assemble the guide but doesn't disclose polyphosphoester in the list of materials. Leong (765 teaches a polyphosphoester material that is intended to be used as a material for a prosthesis. The Leong material has additional advantages such as it is biodegradable and can act as a therapeutic agent delivery device. Additionally Leong does mention this particular material is especially useful in genetic engineering. At the time of the invention it would have been obvious to one having ordinary skill in the art to substitute the Leong material for nerve guides into the Peulve nerve guide system since the Leong material is biodegradable and useful for delivery of therapeutic agents.

Regarding claims 24-26, Leong discloses that the molecular weight of the polyphoester can be any weight from 2000- 10^6 daltons.

Regarding claims 27 and 28, the combined Peulve device discloses all of claim 22, but doesn't disclose the porosity of the material. However, it is well known in the art to vary the porosity of a material to change the amount of time the material takes to dissolve invitro. At the time of the invention it would have been obvious to one having ordinary skill in the art to make the porosity 8% or 35% to modify the amount of time the material requires for complete dissolution.

Regarding claims 30 and 31, the combined Peulve device discloses a nerve with a 1.5 mm diameter.

Regarding claim 40, the Peulve-Leong device discloses ('828 (Paragraph 00411) the use of a complex of DNA and a cationic polymer or lipid loaded into a cuff.

Regarding claim 56, the Peulve-Leong device discloses that BDNF ('828 (Paragraph 0241) is used in the gene delivery system of Peulve.

Regarding claims 48 and 49, the protein delivery system comprises microspheres that contain protein wherein said protein will be inherently released from the microspheres progressively. The microspheres are made from a poly(phosphoester) polymer.

Regarding claim 54, Leong discloses the nerve conduit should release protein from the microspheres, but does not disclose for what temporal duration the microspheres should release the protein. Providing the nerve cells with a long, constant source of protein will improve the regenerative qualities of the procedure. At the time of the invention it would have been obvious to one having ordinary skill in the art to modify the Peulve-Leong device so that microspheres will dissolve very slowly thus releasing the protein for three months or longer, and thereby improving the regenerative qualities of the procedure. Also, methods of modifying the longevity of the microspheres are well known in the art. Increasing porosity or surface area of the sphere will result in faster dissolution times.

Regarding claim 55, the Peulve-Leong device doesn't disclose the length of protein to be loaded per length of conduit. It would have been an obvious matter of design choice to modify the Peulve-Leong device to have the 10 microns of protein to be loaded per 10 mm of conduit since the applicant has not disclosed this loading procedure would solve any stated problem or is for any particular purpose and it appears that the undisclosed amount of protein added by Peulve would perform equally well.

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11. Claims 32-38, 98, and 108-114 are rejected under U.S.C. 103(a) as being obvious over Peulve et al. '828 in view of Leong '765, as applied above, further in view of Li '381.

Regarding claims 32-33, the combined Peulve device discloses a nerve guide. Neither Peulve nor Leong disclose the wall thickness of the nerve guide, but nerve guide conduits typically have a wall thickness of about 0.3mm (which includes thicknesses from .21 mm to .39mm). Li teaches the thickness of nerve guides, "Typically for a 1 mm x .5cm conduit having an overall wall thickness of about .3mm. . ." At the time of the invention it would have been obvious to one having ordinary skill in the art to make the wall thickness of the Leong device about .3 mm because Li teaches this size is the typical size of a nerve guide.

Regarding claims 34-37, the combined Peulve device discloses a device with many layers of material (figure 1 of Li shows a multi-layered material). The Peulve device inherently has a multilayered wall. A collagen wall for a nerve guide appears as shown as Li. The thickness of the individual layers is not disclosed. It would have been an obvious matter of design choice to modify the Leong-Li device to have a wall layer thickness of 25 micrometers since the applicant has not disclosed the layer thickness of 25 micrometers would solve any stated problem or is for any particular purpose and it appears that the undisclosed layer thickness of Li would perform equally well.

Regarding claim 38, the combined Peulve device discloses the claimed invention except for the outer surface of the wall has a greater microporosity than the luminal surface of the conduit. Li '381 teaches making a conduit with an outer layer that is more porous than the inner layer and provides motivation to apply this technique on other nerve guides (see column 4, last paragraph.) Li designs the nerve guide to have this configuration to instill mechanical strength to the guide, while maintaining the benefit of a highly porous material.

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At the time of the invention it would have been obvious to one having ordinary skill in the art to modify the Peulve-Leong device to have an outer surface of the wall that has a greater microporosity than the luminal surface of the conduit to instill mechanical strength to the guide, while maintaining the benefits of a highly porous material.

12. Claims 41 and 117 is rejected under 35 U.S.C. 103(a) as being obvious over Peulve et al. 2002/0071828 in view of Leong '092, as applied above, further in view of PG-PUB 2002/0044972 to Davis et al.

Regarding claim 41 the Peulve-Leong device discloses the nerve guide contains DNA particles but doesn't disclose the size of the complex's particles. The applicant has not disclosed any criticality for the size of the particles. It would have been an obvious matter of design choice to modify the Peulve device to have a DNA particle size of 20nm since the applicant has not disclosed the size of the particles would solve any stated problem or is for any particular purpose and it appears that the DNA particles of Peulve and Leong would perform equally well. Additionally, Davis et al. 2002/0044972 teaches a method and motivation to reduce DNA particle size into a range of 1000nm to 10nm, to enable DNA to more easily enter the target cells. At the time of the invention it would have been obvious to one having ordinary skill in the art to reduce the DNA particles of the combined Peulve device to 20nm to enable the DNA to more easily enter the target cells as taught by Davis et al.

13. Claims 52, 53, 128 and 129 are rejected under U.S.C. 103(a) as being obvious over Peulve '828 in view of Leong '765, as applied above, further in view of PG-PUB 2002/0009493 to Schwendeman et al.

The combined Peulve device discloses the use of microspheres in a protein delivery system but does not suggest the size of microspheres. The applicant has not disclosed any criticality for the size of the microspheres. It would have been an obvious matter of design choice to modify the Peulve device to have a microsphere size of 10um since the applicant has not disclosed the size of the particles would solve any stated problem or is for any particular purpose and it appears that the microspheres of Peulve and Leong would perform equally well. Additionally, Schwendeman et al teaches a method and motivation to use microspheres for protein delivery with a 10 um to 100um size. The purpose of using very small particles is to help insure continuous, gradual release of protein into the target cells. At the time of the invention it would have been obvious to one having ordinary skill in the art to modify the combined Peulve device to use microspheres of about 10um to enable the microspheres to gradually release protein into the target cells.

Response to Arguments

14. Applicant's arguments filed 08 January 2004, 05 March 2004, and 30 November 2004 have been fully considered but they are not persuasive.

15. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

This application is claiming the benefit of a prior filed nonprovisional application under 35 U.S.C. 120, 121, or 365(c). Copendency between the current application and the prior application is required.

Since, Applicant is not entitled to receive the benefit of the earlier filing date of U.S. Patent Nos. 6,238,687 and 5,912,225. These references have not been overcome and thus are still considered to be prior art.

16. The declaration filed 08 January 2004 is insufficient to overcome PG-PUB 2002/0155092 and U.S. Patent No. 6,485,737 since the claims are directed to nerve guides and applicant only declares that he invented phosphorous containing polymers. In addition, the art is still applicable under 103(a), since the references were not owned by the same person or subject to an obligation of assignment to the same person. See MPEP 706.02(l)(1).

17. Applicant argues that the use of poly(phosphoester) compounds has unexpected results when used in nerve tissues. MPEP 716(C) states: The arguments of counsel cannot take the place of evidence in the record. Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

Conclusion

18. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on

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the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

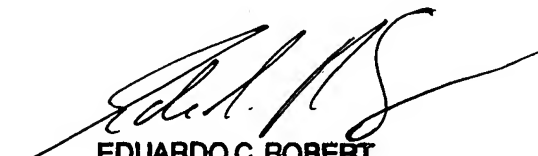
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica R. Baxter whose telephone number is 571-272-4691. The examiner can normally be reached on M-F 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eduardo Robert can be reached on 571-272-4719. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


jrb

Jessica R Baxter
Examiner
Art Unit 3731


EDUARDO C. ROBERT
PRIMARY EXAMINER